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08/765837

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September 15, 2005

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Re: Title: ANTIGENIC POLYPEPTIDE SEQUENCE OF FACTOR VIII, FRAGMENTS AND/OR EPITOPES THEREOF
Letters Patent No. 6,866,848
Issued: March 15, 2005
Our Reference: VANMA48.001APC

Dear Sir:

Enclosed for filing is a Certificate of Correction in connection with the above-identified patent. For your convenience, attached is a copy of an Amendment filed February 24, 2004 in which the subject word is highlighted.

As the errors cited in the Certificate of Correction were incurred through the fault of the Patent Office, no fee is believed to be required. However, please charge our Deposit Account No. 11-1410 for any fees that may be incurred with this request.

Respectfully submitted,

Knobbe, Martens, Olson & Bear, LLP

Marina L. Gordey
Registration No. 52,950
Customer No. 20,995

Enclosures

1923667
090905

UNITED STATES PATENT AND TRADEMARK OFFICE
CERTIFICATE OF CORRECTION

PATENT NO. : 6,866,848

DATED : March 15, 2005

INVENTOR(S): Laub et al.

It is certified that error appears in the above-identified patent and that said Letters Patent is hereby corrected as shown below:

In claim 1, line 46, please delete "threomine" and insert therefore --threonine--

MAILING ADDRESS OF SENDER:

Marina L. Gordey
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2040 Main Street, 14th Floor
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PATENT NO. 6,866,848

September 15, 2005

VANMA48.001APC
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SEP 27 2005

41 Docket No.: VANMA48.001APC **Customer No.: 20,995**

1644

AMENDMENT / RESPONSE TRANSMITTAL

Applicant	:	Laub et al.
App. No.	:	08/765,837
Filed	:	September 7, 1999
For	:	ANTIGENIC POLYPEPTIDE SEQUENCE OF FACTOR VIII, FRAGMENTS AND/OR EPITOPES OF THIS SEQUENCE
Examiner	:	Nolan, Patrick J.
Art Unit	:	1644

CERTIFICATE OF MAILING

I hereby certify that this correspondence and all marked attachments are being deposited with the United States Postal Service as first-class mail in an envelope addressed to: Commissioner for Patents, P.O. Box 1450, Alexandria, VA 22313-1450, on

February 24, 2004
(Date)

Daniel Hart
Daniel Hart, Reg. No. 40,637

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Sir:

Transmitted herewith for filing in the above-identified application are the following enclosures:

(X) Amendment and Response to Office Action in 7 pages.

The fee has been calculated as shown below:

FEE CALCULATION				
FEE TYPE		**FEE CODE**	**CALCULATION**	**TOTAL**
Total Claims	19 - 0 = 0	1202 ($18)	0 x 18 =	$0
Independent Claims	5 - 4 = 1	1201 ($86)	1 x 86 =	$86
Multiple Claim		1203 ($290)		$0
1 Month Extension		1251 ($110)		$
2 Month Extension		1252 ($420)		$
3 Month Extension		1253 ($950)		$
			TOTAL FEE DUE	**$86**

(X) A check in the amount of $86 is enclosed.

(X) Return prepaid postcard.

(X) Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Daniel Hart

Daniel Hart
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Customer No. 20,995
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SEP 27 2005

VANTA48.001APC

PATENT

IN THE UNITED STATES PATENT AND TRADEMARK OFFICE

Applicant	:	Laub et al.
Appl. No.	:	08/765,837
Filed	:	September 7, 1999
For	:	ANTIGENIC POLYPEPTIDE SEQUENCE OF FACTOR VIII, FRAGMENTS AND/OR EPITOPES OF THIS SEQUENCE
Examiner	:	Nolan, Patrick J
Group Art Unit	:	1644

AMENDMENT AND RESPONSE TO OFFICE ACTION

Commissioner for Patents
P.O. Box 1450
Alexandria, VA 22313-1450

Dear Sir:

In response to Office Action mailed November 25, 2003, please amend the above-identified application as follows.

Amendments to the Claims are reflected in the listing of claims which begins on page 2 of this paper.

Summary of Interview begins on page 6 of this paper.

Remarks/Arguments begin on page 7 of this paper.

AMENDMENTS TO THE CLAIMS

1-30. **Cancelled**

31. **(Currently amended)** An isolated antigenic fragment of the human Factor VIII polypeptide of SEQ ID NO: 21, said fragment comprising at least 7 amino acids of a human Factor VIII fragment selected from the group consisting of a human Factor VIII fragment extending from arginine 1652 to arginine 1696 inclusive, a human Factor VIII fragment extending from threonine 1739 to tyrosine 1748 inclusive (SEQ ID NO: 3), a human Factor VIII fragment extending from asparagine 1777 to phenylalanine 1785 inclusive (SEQ ID NO: 4), a and a human Factor VIII fragment extending from glutamic acid 1885 to arginine 1917 inclusive.

32. **(Currently Amended)** The isolated antigenic ~~polypeptide~~ fragment according to Claim 31, wherein said human Factor VIII fragment comprises an epitope selected from the up consisting of: a human Factor VIII fragment extending from arginine 1652 to tyrosine 1664 (SEQ ID No: 1), a human Factor VIII fragment extending from threonine 1739 to tyrosine 1748 (SEQ ID No: 3), a human Factor VIII fragment extending from asparagine 1777 to phenylalanine 1785 (SEQ ID No: 4), a human Factor VIII fragment extending from glutamic acid 1885 to phenylalanine 1891 (SEQ ID No: 7), a human Factor VIII fragment extending from glutamic acid 1893 to alanine 1901 (SEQ ID No: 8), and a human Factor VIII fragment extending from aspartic acid 1909 to arginine 1917 (SEQ ID No: 9).

33. **(Currently amended)** The isolated antigenic ~~polypeptide~~ fragment according to Claim 31, wherein said antigenic polypeptide comprises tyrosine or histidine.

34. **(Currently Amended)** An isolated conformational epitope comprising at least two different human Factor VIII fragments of Claim 32, wherein said fragments are positioned in proximity to each other when the protein is folded in its tertiary or quaternary structure to form a conformational epitope which is recognized by an inhibitor of Factor VIII selected from the group consisting of B lymphocytes, MHC I proteins, MHC II proteins, and anti-Factor VIII antibodies.

35. **(Currently Amended)** An isolated conformational epitope comprising at least two different epitopes from a fragment of the human Factor VIII polypeptide of SEQ ID NO: 21 wherein said fragment is selected from the group consisting of a human Factor VIII fragment extending from arginine 1652 to arginine 1696 inclusive, a human Factor VIII fragment

extending from threonine 1739 to aspartic acid 1831, inclusive, and a human Factor VIII fragment extending from glutamic acid 1885 to arginine 1917 inclusive.

36. **(Currently Amended)** A complex, comprising a carrier protein or a carrier peptide linked to the ~~polypeptide~~ fragment of Claim 31 or the conformational epitope of Claim 35, wherein said complex has higher immunogenicity than said polypeptide of Claim 31.

37-38. **(Cancelled)**

39. **(Currently amended)** A pharmaceutical composition comprising at least the antigenic ~~polypeptide~~ fragment of Claim 31, or the conformational epitope of Claim 35 and an acceptable pharmaceutical vehicle.

40-43. **(Canceled)**

44. **(Previously presented)** The complex of Claim 36, wherein said carrier protein or said carrier peptide are bovine serum albumin or hemocyanin.

45. **(Currently amended)** An isolated polypeptide, consisting of a fragment of the human Factor VIII polypeptide of SEQ ID NO: 21, wherein said fragment is selected from the group consisting of a human Factor VIII fragment between arginine 1652 and arginine 1696 inclusive, ~~a human Factor VIII fragment between threonine 1739 and aspartic acid 1831 inclusive, and~~, a human Factor VIII fragment between glutamic acid 1885 and arginine 1917 inclusive, and a fragment comprising at least 7 amino acids thereof, wherein said polypeptide is antigenic.

46. **(Previously presented)** A pharmaceutical composition, comprising the antigenic polypeptide of Claim 45 and an acceptable pharmaceutical vehicle.

47. **(Previously presented)** A complex, comprising a carrier protein or a carrier peptide linked to the antigenic polypeptide of Claim 45, wherein said complex has higher immunogenicity than said polypeptide of Claim 45.

48. **(Previously presented)** The complex of Claim 47, wherein said carrier protein or said carrier peptide are bovine serum albumin or hemocyanin.

49. **(Previously presented)** A conformational epitope comprising at least two different human Factor VIII fragments of Claim 45, wherein said fragments are positioned in proximity to each other when the protein is folded in its tertiary or quaternary structure to form a conformational epitope which is recognized by an inhibitor of Factor VIII selected from the

group consisting of B lymphocytes, MHC I proteins, MHC II proteins, and anti-Factor VIII antibodies.

50. **(Currently amended)** An isolated ~~The~~ polypeptide ~~according to Claim 45~~, consisting of a fragment of the human Factor VIII polypeptide of SEQ ID NO: 21, wherein said human Factor VIII fragment consists of an epitope selected from the group consisting of: a human Factor VIII fragment contained between arginine 1652 and tyrosine 1664 (SEQ ID No: 1), a human Factor VIII fragment contained between threonine 1739 and tyrosine 1748 (SEQ ID No: 3), a human Factor VIII fragment contained between asparagine 1777 and phenylalanine 1785 (SEQ ID No: 4), a human Factor VIII fragment contained between glutamic acid 1794 and tyrosine 1815 (SEQ ID No: 5), a human Factor VIII fragment contained between methionine 1823 and aspartic acid 1831 (SEQ ID No: 6), a human Factor VIII fragment contained between glutamic acid 1885 and phenylalanine 1891 (SEQ ID No: 7), a human Factor VIII fragment contained between glutamic acid 1893 and alanine 1901 (SEQ ID No: 8), and a human Factor VIII fragment contained between aspartic acid 1909 and arginine 1917 (SEQ ID No: 9), wherein said polypeptide is antigenic.

51. **(Previously presented)** A pharmaceutical composition, comprising the antigenic polypeptide of Claim 50 and an acceptable pharmaceutical vehicle.

52. **(Previously presented)** A complex, comprising a carrier protein or a carrier peptide linked to the antigenic polypeptide of Claim 50, wherein said complex has higher immunogenicity than said polypeptide of Claim 45.

53. **(Previously presented)** The complex of Claim 52, wherein said carrier protein or said carrier peptide are bovine serum albumin or hemocyanin.

54. **(Previously presented)** A conformational epitope comprising at least two different human Factor VIII fragments of Claim 50, wherein said fragments are positioned in proximity to each other when the protein is folded in its tertiary or quaternary structure to form a conformational epitope which is recognized by an inhibitor of Factor VIII selected from the group consisting of B lymphocytes, MHC I proteins, MHC II proteins, and anti-Factor VIII antibodies.

55. **(New)** An isolated polypeptide, consisting of a fragment of the human Factor VIII polypeptide of SEQ ID NO: 21, wherein said fragment is threonine 1739 to aspartic acid 1831, wherein said polypeptide is antigenic.

SUMMARY OF INTERVIEW

Identification of Claims Discussed

Applicants thank the Examiner for extending the courtesy of a telephonic interview to Applicants' representatives on Feb. 2, 2004. During the interview, Claims 31-36, 39, 45-54, and new Claim 55 submitted herewith were discussed.

Proposed Amendments

The discussed amendments are incorporated into the section "**AMENDMENTS TO THE CLAIMS**" of the present Response to the Office Action.

Results of Interview

As provided in the Interview Summary mailed Feb. 5, 2004, the Examiner indicated that the Amendments submitted herewith would overcome all the remaining rejections. The Examiner also indicated that an updated search would be conducted prior to allowance.

REMARKS

Claims 31-36, 39, 45 and 50 have been amended. Support for the amendments can be found in the specification as filed, for example, on page 17, lines 23-24, on page 21 lines 10-14. No new matter has been introduced with the amendments. New Claim 55 has been added. Support for the new claim can be found in Claim 45 as filed on June 24, 2003. As a result, claims 31-36, 39 and 44-55 are pending. The following addresses the substance of the Office Action.

Claim Rejection under 35 U.S.C. §112

The Examiner has rejected claims 32, 33, 34, 36, 39 and 44 under 35 U.S.C. §112, second paragraph, for being indefinite. More specifically, the Examiner asserted that Claims 32, 33 and 39 lack antecedent basis for "the antigenic polypeptide of Claim 31"; and Claim 36 lacks antecedent basis for "the polypeptide of Claim 31". The Applicants have now amended Claims 32, 33, 36 and 39 to recite "the isolated antigenic fragment of Claim 31" which is supported by currently amended Claim 31. During the interview of Feb. 2, 2004, the Examiner indicated that this amendment would render the rejection moot. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim rejection under 35 U.S.C. §102

The Examiner has rejected Claims 45-49 under 35 U.S.C. §102(b) as being allegedly anticipated by USP 4,965,199. More specifically, the Examiner alleges that Claims 45-49 read on the disclosed Capon fragment, residues 1799-1860 and its use in a pharmaceutical composition or as a complex with BSA, because the present invention comprises at least 7 amino acid sequences of the recited amino acid fragments as long as the resulting polypeptide fragment is antigenic. During the interview of Feb. 2, 2004, the Examiner indicated that this amendment would render the rejection moot. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Claim objections

The Examiner has objected to Claims 50-54 as being dependent upon a rejected claim. Claim 50 was rejected as being dependent upon a rejected claim. The Applicants have amended Claim 50 into independent form, During the interview of Feb. 2, 2004, the Examiner indicated that this amendment would render the rejection moot. Accordingly, Applicants respectfully request that the rejection be withdrawn.

Allowable subject matter

The Examiner has indicated that Claim 31 is allowable. Claim 35 was indicated as allowable in the previous Office Action Furthermore, during the interview of Feb. 2, 2004, the Examiner indicated that the amendments provided herein would overcome all of the rejections currently of record.

Applicants believe that all outstanding issues in this case have been resolved and that the present claims are in condition for allowance. Nevertheless, if any undeveloped issues remain or if any issues require clarification, the Examiner is invited to contact the undersigned at the telephone number provided below in order to expedite the resolution of such issues.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: Feb. 24 2004

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